IN THE SPECIFICATION

On page 1, lines 1-3 (and elsewhere as appropriate) please replace the present title with the following Title:

--THERAPEUTIC USE OF THE SMR1 PROTEIN AND ACTIVE DERIVATIVES THEREOF

~~THERAPEUTIC USE OF THE SMR1 PROTEIN, THE SMR1 MATURATION PRODUCTS, SPECIFICALLY THE QHNPR PENTAPEPTIDE AS WELL AS ITS BIOLOGICALLY ACTIVE DERIVATIVES~~--.

Please substitute the paragraphs between page 7, line 11 to page 8, line 19, with the following revised paragraphs:

--It has been described that, *in vivo*, SMR1 is selectively processed at pairs of basic amino acid sites in a tissue- and sex-specific manner to give rise to mature peptide products, in a manner similar to the maturation pathway of peptide-hormone precursors (Rougeot et al., 1994). Generally, this selective proteolytic fragmentation has been shown to be critical for the generation and the regulation of biologically active peptides (Lindberg et al., 1991; Steiner et al., 1992). The biosynthesis of the peptides generated from SMR1 or from its human counterpart by cleavage at pairs of arginine residues e.g. the undecapeptide: VRGPRRQHNPR (SEQ ID NO: 7); the hexapeptide RQHNPR (SEQ ID NO: 12); and the pentapeptide: QHNPR (SEQ ID NO: 1), is subject to distinct regulatory pathways depending on 1) the organ: SMG and prostate, 2) the developmental stage: from 6 weeks postnatal, 3) the sex: predominantly in the male, and 4) gonad hormones: the androgens Furthermore, *in vivo*, the mature peptides which accumulate in the male rate SMG, are exported into the extracellular space in response to a specific external stimulus and, in this way are transported within the salivary and blood fluids (Rougeot et al., 1993). The fact that these peptides are mainly produced in postpubescent male rats and are secreted into the saliva and blood under

stimulated conditions, led one to postulate that they have a local and systemic physiological role in mediating some male-specific behavioral characteristics but this role was totally unknown.

SUMMARY AND OBJECTS OF THE INVENTION

The inventors have now discovered that the maturation products of the SMR1 protein, specifically a peptide of structural formula XQHNPR (SEQ ID NO: 14) recognize specific target sites in organs that are deeply involved in the mineral ion concentration. This discovery has led the inventors to assign to the SMR1 pentapeptide, hexapeptide or undecapeptide an active role in the regulation of the metal ion concentrations in the body fluids and tissues, and thus a therapeutic role of these peptides in all the metabolic disorders related to a mineral ion imbalance.

Thus, the present invention concerns the therapeutic use of the peptides of structural formula XQHNPR (SEQ ID NO: 14) wherein X denotes a hydrogen atom or X represents an amino acid chain chosen from the following: X = V or X = VR or X = VRG or X = VRGP or X = VRGPR or X = VRGPRR, for preventing or treating diseases caused by a mineral ion imbalance in a mammal specifically in human.--

Please replace the paragraph on page 30, lines 19-21 with the following paragraph:

--Another object of the present invention comprises a process for screening ligand molecules that possess an antagonist biological activity on the target receptor of the ~~RQHNPR (SEQ ID NOS; 1-7) pentapeptide~~ XQHNPR peptide (SEQ ID NO: 14), comprising the steps of:--

Please replace the paragraph on page 40, lines 7-16, with the following paragraph:

--Thus, the invention also concerns the biologically active derivatives of the XQHNPR (SEQ ID NO: 14) peptide that have been selected according to the screening processes hereinbefore described, provided that they have not the following structure: Y-HNP-Z, wherein Y denotes a glutamine (Q) or a pyroglutamic acid residue and ~~Y~~ Z represents an OH group or a basic amino acid, the basic amino acid being a Lysine (K) or an Arginine (R). Indeed, also excluded, as a member of the biologically active derivatives of the XQHNPR (SEQ ID NO: 14) peptide, is the 146 amino acid protein constituting the SMR1 peptide itself (PCT Patent Application No WO 90/03981). However, the therapeutic use of these molecules that are excluded by themselves of the present invention, is a main object of the instant invention.--